

## Correspondence

### Reversible renal failure after combined treatment with enalapril and frusemide in a patient with congestive heart failure

Sir,

Funck-Brentano *et al* (1986;55:596-8) have reported a case of reversible renal failure occurring in an elderly patient with congestive heart failure after the addition of enalapril to his treatment. We have recently seen two cases of acute renal failure in this setting and two further patients in whom renal impairment developed over a longer period. None had documented hypotension.

Two male patients aged 68 and 66 with histories of longstanding hypertension were admitted with hypertensive left ventricular failure. Initial investigations showed plasma urea concentrations of 14.5 and 14.0 mmol/l respectively. Both men were treated with frusemide (80 mg every morning) and enalapril (10 mg and 5 mg twice a day respectively). Symptoms and blood pressure were controlled without documented hypotension. Within one month, both were readmitted to hospital with deteriorating renal function, and one patient also had biopsy proven toxic epidermal necrolysis. Peak urea and creatinine concentrations were 21.3 mmol/l and 303  $\mu$ mol/l and 42.6 mmol/l and 772  $\mu$ mol/l respectively. Medication was withdrawn, but the patient with epidermal necrolysis was treated with oral steroid. Renal function initially improved in both cases, but both patients died—the first suddenly and the second of uraemia (urea 65.5 mmol/l, creatinine 569  $\mu$ mol/l).

We have since seen two further patients with renal impairment after more prolonged treatment with enalapril. One, a woman aged 78 years, had cardiac failure secondary to ischaemic heart disease and aortic regurgitation. The initial plasma urea concentration was 13.9 mmol/l; eight months later it had risen to 23.4 mmol/l (creatinine 184  $\mu$ mol/l). Tender expansion of the finger pulps and koilonychia also developed. Ten days after the withdrawal of enalapril plasma urea was 13.6 mmol/l and plasma creatinine 160  $\mu$ mol/l. The changes in her finger pulps and nails resolved over several weeks. The other case occurred in a man aged 70 years who had a history of hypertension and arteriopathy. An episode of hypertensive left ventricular failure was controlled with diuretic agents and enalapril; blood urea

was 9 mmol/l and creatinine 149  $\mu$ mol/l. Six months later after readmission with uncontrolled hypertension, left ventricular failure, and oliguria, the blood urea peaked at 65.0 mmol/l and creatinine at 750  $\mu$ mol/l. Enalapril was withdrawn and the hypertension was controlled with nifedipine and methyl-dopa. His urine output and uraemia improved over the next two weeks, but he too died suddenly.

The four patients described above all had renal impairment and had been treated with enalapril and diuretic agents for hypertension or left ventricular failure or both. In two renal function deteriorated sharply and they died from renal failure; in the other two the deterioration was less severe. This does not imply a cause and effect relation in these very ill patients, but such a relation cannot be discounted. Cleland *et al* have reported first dose hypotension with transient renal impairment in a small number of patients with heart failure treated with enalapril<sup>1</sup> and have predicted on theoretical grounds that long term treatment with enalapril may impair renal function in the absence of hypotension.<sup>2</sup> Funck-Brentano *et al* have postulated that sodium depletion may be the link between inhibition of angiotensin converting enzyme and renal failure. Irrespective of the mechanism our observations support those of Funck-Brentano *et al* which lead to the conclusion that caution is needed when enalapril is prescribed in the management of heart failure or in the presence of appreciable renal failure.

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#### References

- 1 Cleland JGF, Dargie HJ, McAlpine H, *et al*. Severe hypotension after first dose enalapril in heart failure. *Br Med J* 1985;291:1309-12.
- 2 Cleland JGF, Dargie HJ, Ball SG, *et al*. Effects of enalapril in heart failure: a double blind study of effects on exercise performance, renal function, hormones, and metabolic state. *Br Heart J* 1985; 54:305-12.